Position Statement on Percutaneous Vertebral Augmentation: A Consensus Statement Developed by the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, American Association of Neurological Surgeons/Congress of Neurological Surgeons, and American Society of Spine Radiology

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Abbreviation: PMMA = polymethylmethacrylate

IT is the position of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, American Association of Neurological Surgeons/Congress of Neurological Surgeons, and American Society of Spine Radiology ("the Societies") that percutaneous vertebral augmentation with vertebroplasty and kyphoplasty is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures when performed in a manner in accordance with published standards (1,2). These procedures are offered only when traditional medical therapy has not provided pain relief or pain is substantially altering the patient's lifestyle. With regard to vertebroplasty, multiple case series (3–17) and retrospective (18,19) and prospective (20–23) nonrandomized studies have shown a statistically significant improvement in pain and function—particularly with regard to ambulation—and these results have been confirmed in a prospective study with use of a control group (24) and in a prospective randomized control study (25). The benefits of vertebroplasty far outweigh its risks and the risks of conservative therapy, and the success rate is consistently high. This procedure is cost-effective because it produces immediate improvement in a patient's quality of life, primarily by means of the alleviation of pain and rapid return to ambulation. In addition to reducing the need for costly skilled care, expensive drugs, or orthopedic devices, a return to ambulation is known to reduce adverse outcomes in elderly patients confined to bed (26).

Kyphoplasty has been introduced as an alternative approach (27). It is similar to vertebroplasty and has been referred to as "balloon-assisted vertebroplasty." Kyphoplasty entails the inflation of a percutaneously delivered balloon in the vertebral body followed by the percutaneous injection of bone cement into the cavity created by the balloon. The balloon is intended to restore the vertebral body height in addition to creating the cavity (27).

After reviewing the published literature on kyphoplasty, the Societies have determined that the clinical response rate in individuals treated with kyphoplasty is equivalent to that seen in patients treated with vertebroplasty. There is no proved advantage of kyphoplasty relative to vertebroplasty with regard to pain relief, vertebral height restoration, or complication rate (27–44).

It is the position of the Societies that vertebral augmentation with vertebroplasty or kyphoplasty is a medically appropriate therapy for the treatment of painful vertebral compression fractures refractory to medical therapy when performed for the medical indi-

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cations outlined in the published standards (1,2). We believe vertebral augmentation with vertebroplasty or kyphoplasty is established therapy and should be reimbursed by payors as a safe and effective treatment for painful compression fractures.

RATIONALE

Vertebral Augmentation versus Traditional Conservative Management

Although "conservative" implies "safe," conservative therapy of vertebral compression fractures is neither benign nor risk-free and its complications are well documented (46–48). Conservative treatment of painful vertebral compression fractures usually consists of bed rest, bracing, and narcotic analgesia. In a recent prospective study of 498 hospitalized patients aged 70 years or older, low mobility (defined as bed rest or ability to transfer to chair) or intermediate mobility (defined as ambulation one to two times with total assistance) were independent predictors of the following poor hospital outcomes at discharge: (*a*) decrease in activities of daily living, (*b*) new institutionalization, and (*c*) death when compared to patients with high mobility (defined as ambulation at least twice with partial or no assistance) (26). The contribution of low mobility to these outcomes remained statistically significant in multivariate analyses, even after controlling for multiple variables including age, sex, severity of illness, and co-morbidities. In short, conservative treatment leads to adverse outcomes associated with low mobility and bed rest, which may be viewed as iatrogenic events leading to complications such as functional decline.

As previously mentioned, conservative treatment often includes immobilization with bed rest. During bed rest, virtually every organ system is adversely affected. These effects tend to be more pronounced in older patients, who have less reserve than younger patients. Bone density decreases approximately 2% per week, a serious concern in patients with osteoporosis, and these patients are unlikely to ever regain the lost bone mass (49). Bone loss tends to occur in stages, with the most dramatic changes occurring in the first 12 weeks of immobilization.

Muscle strength decreases 1%–3% per day or 10%–15% per week (46). Almost half of normal strength is lost within 3–5 weeks of immobilization, and the rate of recovery from disuse weakness is slower than the rate of loss. Complete rest results in decreased endurance and this leads to a sense of fatigue and reduced patient motivation, setting up a vicious circle of greater inactivity. Ligament complexes are also affected by immobilization, leading to contractures, which are more prone to occur in frail, elderly individuals. Muscles that cross two joints, such as the back muscles, are particularly at risk of shortening during immobilization. There is abundant evidence that shows early active mobilization after initial stabilization—a benefit of vertebral augmentation—is the key to the prevention of contracture.

Early mobilization also leads to the prevention of pressure sores, the prevalence of which tends to increase substantially with age. Patients older than 70 years have more than 70% of all pressure sores and get them within 2 weeks of admission to the hospital. Once decubitus ulcers occur, nursing costs can increase by as much as 50%, with the total cost of treatment per ulcer estimated to be between $15,000 and $20,000. Complications often develop with pressure sores. Infection is the most common complication and leads to septicemia, osteomyelitis, anemia, and protein loss by means of chronic discharge.

Cardiovascular effects include increased heart rate, shorter diastolic times, and reduced coronary blood flow. In addition, patients have an overall decrease in cardiac output, stroke volume, and left ventricular function. In the elderly, orthostatic hypotension occurs within the first 3 weeks of bed rest. This, along with the elevated heart rate, leads to diminished diastolic ventricular filling and a decrease in cerebral perfusion. Depending on the length of bed rest, it may take 20–72 days to restore pre–bed rest cardiac function (46).

In patients at bed rest, the frequency of deep vein thrombosis is 61%, with proximal deep vein thrombosis occurring in 29%. Pulmonary embolism is seen in 2%–12% of patients and is fatal in 0.5%–10% (49). A restrictive impairment, an overall decrease in muscle strength, deconditioning of respiratory muscles, and failure to fully expand the chest wall results in a 25%–50% decrease in respiratory capacity (47). In addition, the lungs have decreased ciliary clearance, less effective coughing, atelectasis, and a predilection for pneumonia. Gastrointestinal effects include reduced appetite, constipation, and fecal impaction, all of which are exacerbated by the concomitant use of narcotics. Glucose intolerance is a frequent but often overlooked complication of bed rest and can mimic brittle diabetes (47). Patients are at increased risk of genitourinary calculus formation, incontinence, urinary tract infection, and urosepsis. Even the central nervous system is not immune; patients at bed rest exhibit higher levels of anxiety, depression, insomnia, pain intolerance, sensory deprivation, and balance problems.

Narcotic analgesia is commonly used in conjunction with bed rest in the treatment of acute and chronic nonmalignant musculoskeletal pain (48,50). Adverse drug reactions have been seen in more than 70% of individuals treated with opioids (48), and although most side effects are minor the elderly are more likely to have a severe adverse drug reaction such as confusion. In one study (48), severe adverse drug reactions occurred in more than 10% of patients. A multivariate analysis of the findings showed that the only factor associated with severe adverse drug reactions was advancing age.

Patients who undergo vertebroplasty have consistently shown immediate and considerable improvement in pain and mobility after treatment (3–25). In a recent study of 79 consecutive patients with osteoporotic compression fractures (24), 55 (70%) of whom were treated with vertebroplasty and 24 (30%) of whom were treated with conservative therapy, the vertebroplasty group showed a statistically significant reduction in pain and an improvement in physical functioning at 24 hours compared with the conservative treatment group. In addition, 24% of the patients who underwent vertebroplasty were able to cease all analgesia after 24 hours; none of the patients in the conservative treatment group were able to stop analgesia. These markedly different clinical outcomes at 24 hours to 1 week represent the enormous benefit of vertebro-

plasty over conservative therapy in terms of early mobilization, even though the clinical outcomes for the two groups at 6 weeks, 6 months, and 12 months were the same.

In a trial comparing vertebroplasty with best medical therapy (25), 40 patients with acute (symptomatic for 6 weeks or less) osteoporotic compression fractures were randomized to receive vertebroplasty or conservative therapy, with crossover for the medically treated group allowed at 6 weeks. The vertebroplasty group showed a statistically significant improvement in pain and mobility and a reduction in medication use immediately after vertebroplasty. None of the patients randomized to medical therapy showed significant improvement, and 16 of the 19 patients were offered vertebroplasty. This post–medical therapy vertebroplasty group also showed statistically significant improvement in all three parameters immediately after the procedure. At 12 weeks, both groups showed statistically significant durability of the therapeutic response (25).

It is well documented that the natural history of healing compression fractures is composed of a gradual improvement in pain within 2–12 weeks, with variable return of function (51,52). What is not described as "natural history" is sudden improvement in pain and return in function—the hallmark picture of a positive therapeutic response with vertebroplasty. Most patients enrolled in the initial vertebroplasty studies did not undergo treatment until all noninvasive therapies had been exhausted. These patients acted as their own internal controls because vertebroplasty was performed at a point in their clinical course where if improvement associated with healing was to occur it should have happened. It is therefore unlikely that the rapid, marked improvement in clinical findings after vertebroplasty was associated with the natural course of the disease.

It may also be argued that patients treated medically are just as likely to have a long-term positive outcome similar to that of patients treated with vertebroplasty, a finding noted in the study by Diamond et al (24). Equality in long-term outcomes, however, does not negate the early positive effects of a successful vertebroplasty. The potential complications associated with conservative therapy are most likely to occur early in the course of a patient's immobilization, leading to physiologic losses from which the patient may not recover or resulting in adverse outcomes as seen in the study by Brown et al (26).

Another consideration is that the positive outcomes seen with vertebroplasty are due to the placebo effect. Vertebroplasty reports have consistently shown positive responses in the 80%–90% range for osteoporotic fractures, regardless of cohort demographics, cause of osteoporosis, geographic location, or type of institution (community practice vs academic setting). The question would be laid to rest with the completion of a sham trial. A feasibility study reported in an abstract by Kallmes et al (53) showed that patients could be successfully randomized to vertebroplasty or a sham procedure, but no meaningful clinical information was obtained. This small study was used to obtain National Institutes of Health funding for a multicenter vertebroplasty versus sham procedure trial. A total of 150 patients are to be studied, but the trial has been hampered by enrollment difficulties.

More than 450 articles about vertebroplasty have been published in the past 20 years. Among these articles, approximately 100 studies addressed the clinical outcomes of patients treated with percutaneous vertebroplasty. Without exception, these reports describe vertebroplasty as a successful therapy for the relief of the pain associated with vertebral compression fractures caused by either osteoporosis or tumor involvement. The earliest literature consisted of a small, retrospective, uncontrolled case series introducing the technique and described excellent results for the patients involved (3–8). Since that time, larger case series have been published (9–19). Literature reviews about the efficacy of vertebroplasty have concluded that the procedure, when used in the setting of osteoporotic compression fractures, results in substantial and immediate pain relief, improved functional status, and minimal short-term complications (54–57). Prospective reports (20–23), including nonrandomized and randomized controlled studies (24,25), also showed overwhelming positive responses. The Societies conclude that the evidence supports the statement that vertebroplasty is efficacious in the relief of pain and improvement of mobility associated with acute and subacute compression fractures. Two studies (17,58) showed similar results in chronic fractures up to 2 years in age.

Given the currently available scientific data, the Societies believe that vertebroplasty has been shown to be more effective than continued medical treatment in patients with painful vertebral compression fractures in whom conservative therapy has failed. To deny a patient vertebroplasty in favor of "more of the same" increases the chance of an adverse outcome associated with low mobility and complications associated with bed rest and narcotic analgesia.

As vertebroplasty use became widespread, kyphoplasty was introduced as an alternative approach. Kyphoplasty entails inflation of a percutaneously delivered balloon in the vertebral body followed by percutaneous injection of bone cement into the cavity created by the balloon. Kyphoplasty is similar to vertebroplasty, differing only in the use of the balloon. Indeed, kyphoplasty has been referred to as "balloon-assisted vertebroplasty." The balloon, in theory, is intended to restore the vertebral body height while creating a cavity to be filled with bone cement (27). The balloon (KyphX Inflatable Bone Tamp; Kyphon, Sunnyvale, Calif) has been approved by the U.S. Food and Drug Administration for use as a bone tamp for the reduction of fractures and/or the creation of a void in cancellous bone.

The clinical outcomes data are not as extensive as those for vertebroplasty. The available data (27–40), however, describe the treatment of osteoporotic and some neoplastic (38) fractures and include some prospective nonrandomized data (27,28,34), with one report including a control group of patients treated with conservative therapy (31). To our knowledge, no investigators have compared kyphoplasty with vertebroplasty. As with vertebroplasty, the kyphoplasty reports show substantial pain relief and improved mobility in the great majority of patients in whom conservative therapy has failed. Because of additional equipment, anesthesia, and hospital costs, kyphoplasty is approximately 2.5 times more expensive than

vertebroplasty. It is possible that certain subgroups of patients may derive more benefit from one particular procedure (45). Features that might affect choice of procedure include the degree of compression deformity, age of fracture, and presence of neoplastic involvement; however, the benefits of kyphoplasty relative to vertebroplasty in such subgroups currently remain undefined. With the considerable added financial expense of kyphoplasty, a substantial clinical benefit over vertebroplasty would have to be proved to justify this cost. A convincing benefit to kyphoplasty relative to vertebroplasty can only be proved by comparing outcomes from both procedures in a prospective, randomized study. The Societies recognize, however, that the performance of kyphoplasty instead of vertebroplasty may be due to operator experience or preference. Because the clinical outcomes studies have shown that kyphoplasty has the same benefit as vertebroplasty in patient pain relief and mobility at similar complication rates, it is the Societies' position that it should be considered an alternative procedure to vertebroplasty.

Quality of Life

Not only has vertebroplasty been shown to decrease pain and improve mobility, it also has a positive effect on patients' quality of life. In a recent study, 46 consecutive patients underwent vertebroplasty. At enrollment, all patients completed the Osteoporosis Quality of Life Questionnaire, a validated 35-item, five-domain, seven-point response-option instrument. All five domains of the questionnaire were improved at 2 weeks after the procedure and remained improved at each evaluation point through 6 months (59). Similar quality of life improvements have been shown for kyphoplasty (68).

Complications

Although the complication rate for vertebroplasty is exceedingly low, complications nevertheless do occur. The primary cause of a symptomatic vertebroplasty complication is leakage of polymethylmethacrylate (PMMA) into adjacent structures, although the vast majority of such leaks are completely asymptomatic. This leakage can occur through fracture lines, through areas of cortical destruction, along the needle track, or into the epidural and paravertebral venous complexes (9,60). Acrylic material that has leaked from the vertebral body may cause spinal cord or nerve root compression, resulting in worsening pain and/or neurologic dysfunction. Although migration of small amounts of PMMA through the epidural or paravertebral venous system to the pulmonary vasculature is virtually always clinically insignificant, rare cases of symptomatic pulmonary embolus have been reported (61).

Perivertebral acrylic is usually asymptomatic, although dysphagia from esophageal compression after a cervical vertebroplasty has occurred (10). Other complications that have occurred, as reported in the literature or through personal knowledge, include fracture of the transverse process or pedicle, paravertebral hematoma, epidural abscess, pneumothorax, cerebrospinal fluid leak, seizure or respiratory arrest from oversedation, and death. Patients with severe osteoporosis may sustain rib fractures (11) or sternal fractures from lying prone on the procedure table.

Hemodynamic compromise has been associated with packing of the acetabulum with PMMA during hip replacement surgery. Although transient systemic hypotension during acrylic injection in vertebroplasty has been reported (62), a large retrospective study of the cardiovascular effects of PMMA in patients undergoing vertebroplasty found no generalized association between acrylic injection and systemic cardiovascular derangement (63).

One theoretical complication is thermal injury to adjacent neurologic structures during acrylic polymerization. There have been no clinical reports of this phenomenon and its possibility appears unlikely on the basis of in vitro tests, which showed no substantial increase in spinal canal temperature with vertebroplasty (64), and in vivo animal experiments, which showed no spinal cord damage from PMMA located adjacent to the dural sac in dogs (65).

More often than not, PMMA leakage is asymptomatic, even in malignant lesions. Cotten et al (9) demonstrated acrylic leaks, both venous and cortical, with computed tomography in 29 of 40 patients with osteolytic metastases or myeloma. Although most of these leaks were asymptomatic, two of eight foraminal leaks produced nerve root compression that necessitated decompressive surgery. In a later series, Cotten et al (13) reported one patient out of 258 treated who experienced spinal cord compression that required surgery. Of 13 patients with radicular pain, only three required surgical decompression and 10 responded to local anesthetic infiltration or medical therapy. Deramond et al (12) noted a single transient neurologic complication in 80 patients with osteoporotic fractures. Review of all major vertebroplasty series showed that the complication rate ranges from 1% to 10%; Murphy and Deramond (66) divide it further into 1.3% for osteoporosis, 2.5% for hemangiomas, and 10% for neoplastic disease. Fortunately, most patients with radicular symptoms respond to anti-inflammatory or narcotic analgesics or local anesthetic infiltration; surgical intervention is required in only a minority of cases. Complications are most likely to occur during or immediately after treatment. In two long-term studies, no complications were found in patients followed up at 48 months (19) and 5 years (67). A difference in complication rates between acute and chronic fractures has not been reported.

The issue of increased risk for fracture at an adjacent level has been raised in the literature. Grados and colleagues (19) found a slight, but statistically significant, increased risk of vertebral fracture in the vicinity of a cemented vertebra when compared to a vertebral fracture in the vicinity of an uncemented fracture. However, new fractures after vertebroplasty may actually represent the natural history of osteoporosis rather than a complication of the procedure and further study is necessary.

Complications associated with kyphoplasty are similar to those seen in vertebroplasty. Six major complications in 531 patients (1.1%) treated with kyphoplasty were reported in a multicenter collection of patients, four of which were neurologic complications (40). This complication rate is similar to the 1.3% complication rate

seen in vertebroplasty for osteoporotic fractures (66).

In summary, clinically significant complications for vertebroplasty remain small and are most significant in the treatment of malignant disease. Most respond to short-term medical therapy, and surgery is usually not required. The Societies recommend that all practitioners incorporate indicator thresholds into one's quality improvement program to identify potential problems. Because serious complications of vertebroplasty are infrequent, a review is recommended for all instances of death, infection, and symptomatic pulmonary embolus. Recommended thresholds for complications can be found in the American College of Radiology's "Standards for the Performance of Percutaneous Vertebroplasty" (1) and the Society of Interventional Radiology's "Quality Improvement Guidelines for Percutaneous Vertebroplasty" (2). The Societies are very confident in the validity of the above-mentioned complication data.

In conclusion, it is the position of the Societies that vertebral augmentation with vertebroplasty or kyphoplasty is a medically appropriate therapy for the treatment of painful vertebral compression fractures refractory to medical therapy when performed for the medical indications outlined in the published standards (1,2). We believe vertebral augmentation with vertebroplasty or kyphoplasty is established therapy and should be reimbursed by payors as a safe and effective treatment for painful compression fractures.

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